

Notice of Allowability

Application No.

09/922,652

Applicant(s)

LASKEY ET AL.

Examiner

Gary B. Nickol Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 09-21-2005.
2. ☒ The allowed claim(s) is/are 88,101,102,104,105,107 and 109-111.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☒ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/175,947.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

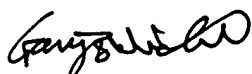
Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____



GARY B. NICKOL, PH.D.
PRIMARY EXAMINER

Gary B. Nickol Ph.D.
Primary Examiner
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EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with B.J. Sadoff on November 17, 2005.

The application has been amended as follows:

88. (Currently Amended) A method of determining the presence or absence of dysplastic or neoplastic cells in a test sample containing cells from an individual, wherein the test sample comprises a specimen selected from the group consisting of a sputum sample, a bronchio-alveolar lavage sample, a urine sample, a breast duct fluid sample, a brushings from the alimentary tract, a cervical cytology sample, and a fecal sample, ~~and a urine sample~~, the method comprising:

contacting the test sample with an antibody or antibody fragment directed against Minichromosome Maintenance protein 2 (MCM2 protein); and

determining the amount of binding of said antibody or antibody fragment to said test sample;

whereby an increase in said amount if detected for the test sample compared with a normal sample is indicative of presence of dysplastic or neoplastic cells in said test sample.

Reasons for Allowance:

The following is an examiner's statement of reasons for allowance:

The closest prior art in the prosecution history of this application is Todorov *et al.* (Laboratory Investigation, Vol. 78, No. 1, 1998, pages 73-78. In response to the obviousness rejection, Applicants have argued (Response, page 8, 09-21-2005) that Todorov *et al.* teaches away from the claimed invention because they teach an overall 27% "false positive" rate of tumor identification when MCM2 was measured in SDS solubilized tissue. It should be further noted that identification of MCM2 in "solubilized" tissue is an *invasive* procedure, as opposed to the non-invasive procedures associated with "cytological" procedures. Cytology is defined as the "science of morphologic examination of individual cells for the purpose of diagnosis" (see Murphy *et al.*, Textbook of Clinical Oncology, page 82, previously cited). Applicants further argue (page 7), that at best, Murphy teaches the detection of tumor markers in histology samples as a means to confirm the clinical relevance of cytomorphologic evaluation. Applicants further argue (page 5, also see specification, pages 7 & 8) that the main reasons that cytological screening fails to detect cervical cancer are the large number of false negatives (10-30%). Hence, applicants argue that this high degree of false positivity in the invasive procedure of Todorov *et al.* would not reasonably have led one of ordinary skill in the art at the time the invention was made to conclude that measurement of MCM2 for *clinical cytological analysis*

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would be as sensitive or specific. These arguments have been carefully considered and are found persuasive. Further, according to MPEP 2145, it is improper to combine references where the references teach away from their combination. In re Grasselli, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir.1983).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN

